REMARKS

These remarks are in response to the Office Action mailed December 2, 2005. Claims 11-13 and 15 were previously withdrawn. Upon entry of the amendment, claims 1-10, 14 and 16-30 are pending and at issue.

I. Rejection Under 35 U.S.C. §102(e)

Claims 1-10, 14 and 16-29 are rejected under 35 U.S.C. § 102(e) as being allegedly anticipated by U.S. Patent No. 6,583,108 to Tamburini et al. (hereinafter, "Tamburini"). Applicants respectfully traverse this rejection.

According to the Office Action, claims 1-10, 14 and 16-29 are under consideration as they pertain to human bikunin, or SEQ ID NO:52 and its use for treatment of emphysema, an obstructive lung disease (COLD). The Office Action states that Tamburini discloses an aerosol and dry powder formulation (claims 2-10 and 20-28) and glycosylated compositions (claim 29), and such compositions will result in "accelerating the rate of mucociliary clearance" (page 2 of the Office Action).

It is submitted, that Tamburini is not an "*enabling disclosure* for making the pharmaceutical compositions containing the human bikunin and its use for treatment of emphysema (page 3 of the Office Action)" as alleged by the Office Action. However, MPEP §2121.01 states that:

> The disclosure in an assertedly anticipating reference must provide an enabling disclosure of the desired subject matter; *mere naming or description of the subject matter is insufficient, if it cannot be produced without undue experimentation.* Elan Pharm., Inc. v. Mayo Found. For Med. Educ. & Research, 346 F.3d 1051, 1054, 68 USPQ2d 1373, 1376 (Fed. Cir. 2003) (At issue was whether a prior art reference enabled one of ordinary skill in the art to produce Elan's claimed transgenic mouse without undue experimentation. Without a disclosure enabling one skilled in the art to produce a transgenic mouse without undue experimentation, the reference would not be applicable as prior art.).

> A reference contains an "enabling disclosure" if the public was in possession of the claimed invention before the date of invention. "*Such possession is effected if one of ordinary skill in the art could have combined the publication's description of the invention with his [or her] own knowledge to make the claimed invention.*" In re Donohue, 766 F.2d 531, 226 USPQ 619 (Fed. Cir. 1985). [emphasis added]

Tamburini, at the time of filing, did not "provide an enabling disclosure of the desired subject matter" because Tamburini merely named or described the subject matter, which "naming and description is insufficient, [since] it cannot be produced without undue experimentation" on the part of one skilled in the art. MPEP §2121.01. For example, there is *only* one instance in Tamburini where "emphysema" is disclosed (col. 18, line 65 of Tamburini). This one instance does not make for an "enabling disclosure" because the public was not put in possession of the claimed invention based on Tamburini. To practice the claimed invention based on Tamburini would require "undue experimentation" by one skilled in the art.

Thus, based on the foregoing discussion, Applicants submit that Tamburini cannot anticipate the claimed invention, because Tamburini does not provide an "enabling disclosure" as under MPEP §2121.01.

Accordingly, withdrawal of the rejection of claims 1-10, 14 and 16-29 under 35 U.S.C. §102(e) is respectfully requested.

III. Rejections Under 35 U.S.C. § 103(a)

Claims 1-10, 13 and 16-30 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Delaria et al. in view of Rasche et al, Fritz et al., O'Riordan et al. and WO93/09233 (hereinafter, "Delaria", "Rasche", "Fritz", "O'Riordan" and '233, respectively). Applicants respectfully traverse this rejection.

According to the Office Action, the prior art allegedly provides the teaching to obtain the human placental bikunin as set forth in SEQ ID NO: 52 (Delaria), the motivation and expectation of success to use the human bikunin in the treatment of emphysema (Fritz; Rasche; and O'Riordan) and cystic fibrosis ('233). Therefore, according to the Office Action, the "prior art provide the teaching and motivation to one of ordinary skill in the art to use fragments of the human bikunin corresponding to one of the two Kunitz domains in glycosylated form... Thus, the prior art provide the motivation, the expectation of success, and the teaching of how to make the composition and its use for the treatment of COLD (paragraph bridging pages 5-6 of the Office Action)".

It is submitted, that it is impermissible to apply the benefit of hindsight in order to arrive at a verdict of obviousness. See, e.g., *Panduit Corp. v. Dennison Manufacturing Co.*, 227 USPQ 337, 343 (Fed. Cir. 1985), vacated & remanded, Dennison Mfg. Co. v. Panduit Corp., 475 U.S. 809, L. Ed. 2d 817, 106 S. Ct. 1578, 229 USPQ 478 (1986), on remand, 810 F2d 1561, 1 USPQ2d 1593 (Fed. Cir. 1987), cert. denied, 107 S. Ct. 2187, 95 L. Ed. 2d 843 (1987), quoting *W.L. Gore Assocs., Inc. v. Garlock, Inc.*, 220 USPQ 303, 313 (Fed. Cir. 1983): It is difficult but necessary that the decision maker forget what he or she has been taught at trial about the claimed invention and cast the mind back to the time the invention was made (often as here many years), to occupy the mind of one skilled in the art who is presented only with the references, and who is normally guided by the then-accepted wisdom in the art.

It is also submitted that MPEP §2121 applies to an obviousness rejection. MPEP §2121 states that: [T]he level of disclosure required within a reference to make it an "enabling disclosure" is the same no matter what type of prior art is at issue. It does not matter whether the prior art reference is a U.S. patent, foreign patent, a printed publication or other. There is no basis in the statute (35 U.S.C. 102 or 103) for discriminating either in favor of or against prior art references on the basis of nationality. *In re Moreton*, 288 F.2d 708, 129 USPQ 227 (CCPA 1961). MPEP §2121.

The Office Action states that "any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill in the time the claimed invention was made, and does not include knowledge gleaned *only* from the applicant's disclosure, such a reconstruction is proper (page 6 of the Office Action)".

It is submitted, however, that it is the claimed invention which describes human bikunin for the treatment of chronic obstructive lung diseases, e.g., emphysema, and not any of the aforementioned art references cited above. According to the Office Action, *only* Fritz discloses Inter-α_1-protease inhibitor for "treatment of diseases related to excess activity of neutrophil elastase such as emphysema (page 4 of the Office Action)". However, Fritz discloses treatment of emphysema only generally, for example in the second paragraph of the Background of the Invention, Fritz states:

> When proteases reach the extracellular space they are normally rapidly trapped by potent endogenous proteinase inhibitors such as α_1-proteinase inhibitor (Travis & Salvesen, *Ann. Rev. Biochem.*, 52, 655, 1983). In certain situations this protective mechanism may not operate or at least not operate adequately, and the consequence may be serious pathological states such as the development of *emphysema*, septic shock, shock lung, ARDS, rheumatoid arthritis, coagulation disorders, kidney and liver failure, inter alia. Proteinase inhibitors with a specific action are of special interest in this connection as potential therapeutics. The proteinase inhibitors which are of particular interest for use in humans have amino acid sequences similar to natural human inhibitors. This particularly applies to

> long-term therapies such as the treatment of α_1-proteinase inhibitor deficiencies (development of *emphysema*) to prevent toxic or allergic side effects. [emphasis added; col. 1, lines 24-41]

It is submitted that the above passage is the only instance where "emphysema" is disclosed. These two instances alone cannot be said to suggest or motivate one skilled in the art to use a different protease, human bikunin, to treat a COLD, e.g., emphysema. In fact, there is *no other* suggestion or motivation in Fritz indicating that effective treatment of a COLD by any protease inhibitor is even possible. Hence, Fritz is not an "enabling disclosure" under MPEP §2121. Secondly, one skilled in the art reviewing Fritz would not understand or imply that all protease inhibitors function to treat chronic obstructive lung diseases. One skilled in the art understands that such conclusions are not made in the absence of some "suggestion or motivation". That is, one skilled in the art would not glean from Fritz that all protease inhibitors function to treat COLD. Hence, Fritz is similar to Tamburini, in that the two instances where Fritz discloses the term "emphysema" cannot be said to suggest or motivate one skilled in the art to use bikunin to treat emphysema. Again, Fritz is not an "enabling disclosure". Fritz combined with the other references do not make for an "enabling disclosure". If there is no suggestion or motivation in Fritz, which is the only reference which discloses the term "emphysema", then there cannot be any suggestion or motivation to combine Fritz with any of the above references. Thus, the references combined do not disclose every aspect of the claimed invention and they are collectively not "enabling disclosures" under MPEP §2121. Applicants maintain that it is the present invention which describes use of human bikunin for treatment of COLD, and *not* Fritz alone or combined with Delaria, Rasche, and O'Riordan.

Also, Fritz, Delaria, Rasche, and O'Riordan combined with the '233 application do not disclose human bikunin for treatment of cystic fibrosis (claim 30). The '233 application discloses that KPI can be used to treat various disease associated with excessive protease activity. One skilled in the art would not consider this to be suggestive or motivating. Thus, similar to the above discussion, there is no suggestion or motivation to combine the '233 application with that

of the above cited references. Also, the references combined do not disclose every aspect of the claimed invention because they are collectively not "enabling disclosures" under MPEP §2121.

Therefore, impermissible use of hindsight has been improperly applied, and the combined references cannot render the claimed invention obvious because alone or combined they do not suggest or motivate the claimed invention and are not "enabling disclosures" under MPEP §2121.

Accordingly, withdrawal of the rejection of claims 1-10, 13 and 16-30 under 35 U.S.C. §103(a) is respectfully requested.

CONCLUSION

Applicants submit that the pending claims are in condition for allowance. Reexamination, reconsideration, withdrawal of the rejections, and early indication of allowance are requested respectfully. If any questions remain, the Examiner is urged to contact the undersigned below.

Check No. 582090 in the amount of $1,020.00 is attached as fee for the Three-month Extension of Time fee. If any additional fees are due, the Commissioner is hereby authorized to charge any fees that may be required by this paper to Deposit Account No. 07-1896. A duplicate copy of the Transmittal Sheet is attached.

Respectfully submitted,

Date: June 2, 2006

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